NYSDOH BUREAU OF TB CONTROL

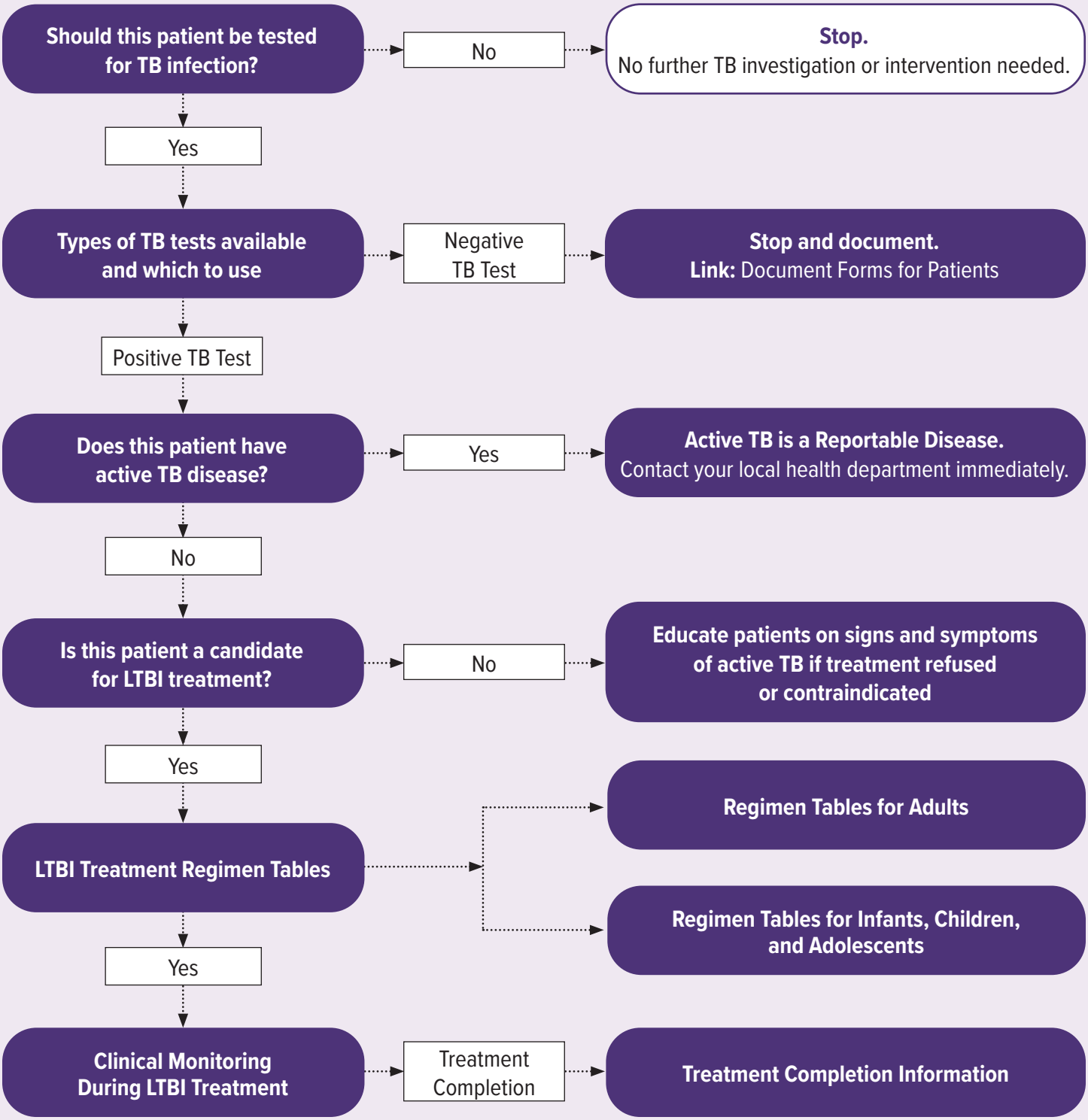
Latent Tuberculosis Infection (LTBI) Electronic Toolkit

Version 2: Updated 11/10/2023

NEW YORK STATE | Department of Health

LTBI FLOW CHART

Click any of the purple buttons to read more



Click the buttons below for:

ICD-10 Codes

Patient Education Resources

Contact your local health department's TB program for consultation as needed

References

Should this Patient be Tested for TB Infection?

Screening Process

Follow these principles when assessing risk for TB disease and testing for LTBI:

All adults and children should receive a TB risk factor assessment at least once as part of their routine primary care:

- Screen persons for new risk factors at subsequent preventive health visits.
- If new TB risk factors are identified since a person's last negative TB test, retest.

Test only persons at risk:

- It can simplify treatment decisions. Testing low-risk persons can result in unnecessary evaluations and treatment.
- Most persons with a risk factor and a positive TB test result should be treated for LTBI.

Examples of new risk factors include the following events and conditions:

- New close contact to a patient with infectious TB disease
- Residence or travel in a high-incidence country for an extended time (>1 month)
- New or anticipated immunosuppressive therapy

Certain people should be tested for TB infection because they are at higher risk for being infected with TB bacteria, including:

- People who have spent time with someone who has TB disease
- Travel to, or residence in a country with an elevated TB rate for at least 1 month. Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe
- People who live or work in high-risk settings (for example: correctional facilities, and homeless shelters)
- Health-care workers who care for patients at increased risk for TB disease
- Infants, children, and adolescents exposed to adults who are at increased risk for latent tuberculosis infection or TB disease

(Center for Disease Control (CDC), *LTBI: A Guide for Primary Health Care Providers Guides & Toolkits* 2021)
(CDC, Tuberculosis (TB) Disease and Latent TB Infection: Symptoms, Risk Factors & Treatment 2021)
(National Society of Tuberculosis Clinicians, *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations 2021*)

Groups at Risk for Developing TB

TB Background and Details

Return to LTBI Flow Chart

Should this Patient be Tested for TB Infection?

Background and Details

What is tuberculosis (TB)?

- TB is a disease caused by bacteria. It usually attacks the lungs but can affect any part of the body.
- People with latent TB infection (LTBI) can have TB bacteria in their body for years before getting sick with active TB disease and becoming contagious.
- Getting tested and treated for LTBI can prevent your patient from developing active TB disease in the future.

How is TB spread?

- TB is spread from one person to another through the air. When a person sick with TB coughs, speaks, or sings, those around them can breathe in the TB bacteria and get infected.

When should the patient get tested for TB?

- If the patient has symptoms of TB (for example, coughing for 3 weeks or more or coughing up blood, heavy sweating at night, feeling very tired, fever or chills, loss of appetite, or unplanned weight loss).
- If the patient has spent a lot of time around someone with TB.
- If the patient takes certain medications or has a medical condition, such as HIV or cancer, that can weaken the immune system.
- If the patient was born in or has traveled to or lived in a country (for 1 month or longer) where many people have TB.

How does the patient get tested and treated for LTBI?

- The patient can get a blood test. Blood tests for LTBI are not affected by previous TB vaccination (Bacille Calmette-Guérin [BCG]).
- If the test for TB infection is positive, check for active TB disease using a chest x-ray and other tests.
- If the patient has active TB disease, refer them for further evaluation and treatment.

(NYC Health, City Health Information: Testing and Treating for Latent Tuberculosis Infection 2021)

Should this Patient Be Tested for TB Infection?

Return to LTBI Flow Chart

Types of TB Tests and Which to Use

Testing

Test individuals with risk factors for TB infection or host risk for progression to TB disease. Testing is not recommended in those without risk factors. There are two types of tests for TB infection: the TB skin test (TST/Mantoux, also formally known as "PPD") and the TB blood test (IGRA/ interferon-gamma release assay).

LTBI diagnosis is based on tuberculin skin test (TST) or interferon-gamma release assay (IGRA) result and exclusion of TB disease:

- Neither test can distinguish between LTBI and TB disease.
- A negative result for either or both tests do not exclude LTBI or TB disease
- Test results may remain positive for the patient's lifetime, even after treatment for LTBI

Recommendation for type of test in adults

- IGRAs are generally preferred though TST is acceptable; test selection may depend on availability, logistics and resources.
- IGRAs are strongly preferred in BCG-vaccinated persons and those who are unlikely to return for interpretation of the TST result

Recommendation for type of test in children

- In children younger than 2 years of age TST is preferred, but an IGRA is acceptable
- IGRAs are preferred for:
  — Children 2 years of age or older, especially for those who have received BCG
  — Children of any age who are unlikely to return for the TST reading

Tuberculin Skin Test (TST)

The Mantoux tuberculin skin test (TST) is also called the TB skin test (formally known as "PPD"). The TST is used to determine if a person has been infected with *M. tuberculosis*. The skin test is administered intradermally using the Mantoux technique by injecting 0.1 ml of 5 tuberculin units of purified protein derivative (PPD) solution. The reading and interpretation of TST reactions should be conducted within 48–72 hours after administration.

(Ahamed et al., *Management of Latent Tuberculosis Infection in Children and Adolescents* 2019)
(CDC, Tuberculin Skin Test Fact sheets 2020)
(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)

Patient Education Resources
Chart Comparing TST vs. IGRA
Chart Interpreting IGRA Result
Interpreting a TST Reactions
IGRAs Available in the United States

Return to LTBI Flow Chart

Does this Patient have Active TB Disease?

Evaluate for Active Disease

A patient with a positive test result for TB infection should be evaluated for active TB disease before starting treatment for LTBI.

To exclude active TB disease, the following should occur:

- A detailed medical history
- Symptom review
- Focused physical examination
- Chest radiography
- Other studies based on history or physical
- Microbiological testing, if indicated

LTBI diagnosis is based on IGRA or TST result and exclusion of TB disease. Evaluate for TB disease before initiating LTBI treatment.
Important: As part of the medical evaluation, a chest radiograph should be performed. LTBI treatment should only be prescribed if the chest radiograph is normal (i.e., no findings consistent with TB disease). If any abnormalities consistent with TB disease are identified or if the patient is symptomatic, the patient should have 3 sputum specimens collected for acid-fast bacilli (AFB) smear and culture. LTBI treatment should only be administered after all 3 cultures are negative. Treating TB disease with an LTBI regimen can lead to drug resistance.
Patients at increased risk of developing active TB disease generally will be treated for LTBI and followed until treatment is completed.
Report persons with suspected active TB disease to the state or local TB program.

(CDC, *Diagnosing latent TB Infection & TB Disease* 2016)
(CDC, *LTBI: A Guide for Primary Health Care Providers Guides & Toolkits* 2021)
(CDC, Core Curriculum on TB 2021)

Differentiating Between LTBI and TB

Return to LTBI Flow Chart

Treatment Considerations

Individuals who have untreated LTBI have a 5-10% chance of getting active TB over a lifetime. LTBI treatment is an effective measure to prevent the progression to active TB disease. When talking to your patient discuss the benefits of preventative treatment and the importance of adherence to the treatment regimen. Most patients will tolerate the treatment medications well.

Topics to consider and possibly discuss with your patients:

- The decision to recommend LTBI treatment is made based on the patient's risk of developing active TB versus the risk of an adverse event from treatment.
- Review the patient's current medical conditions and medications against the list of known contraindications and drug interactions of LTBI medications and regimens.
- Counseling the patient in his or her preferred language, using a medical interpreter when needed, is important.
- Education and counseling should support a patient-centered approach that emphasizes shared decision making.
- The rationale for taking a medication with potential toxicity to prevent a possible future event when a patient currently feels well can be difficult to understand.

(CDC, Core Curriculum on TB 2021)
(National Society of Tuberculosis Clinicians, *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations* 2021)

Directly Observed Therapy (DOT)

Patient Education, Adherence, and Support

Patient Education Resources

Return to LTBI Flow Chart

LTBI Treatment Regimens

If short-course treatment regimens are not a feasible or an available option, 6 to 9 months of isoniazid monotherapy (6H/9H) are alternative, effective latent TB infection treatment regimens. Although effective, 6H and 9H have higher toxicity risk and lower treatment completion rates than most short-term treatment regimens.

All treatment must be modified if the patient is a contact of an individual with drug-resistant TB disease. Clinicians should choose the appropriate treatment regimen based on drug susceptibility results of the presumed source case (if known), coexisting medical conditions (e.g., HIV), and potential for drug-drug interactions. Consultation with a TB expert is advised if the known source of TB infection has drug-resistant TB.

Short-course treatment regimens are effective, safe, and have higher completion rates than longer 6H and 9H Shorter, rifamycin-based treatment regimens generally have a lower risk of hepatotoxicity than 6H and 9H. Two examples are 3 months of isoniazid and rifapentine once weekly (3HP), or 4 months of rifampin daily (4R).

Consider checking for medication shortages prior to prescribing medication.
FDA Drug Shortage: https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages
(CDC, *Treatment regimens for latent TB infection* 2020) https://www.cdc.gov/tb/topic/treatment/ltbi.htm

Infant, Child, or Adolescent Treatment Regimen
Adult Treatment Regimen
Formulation and Special Considerations for Pediatric Patients
Treatment Completion

Return to LTBI Flow Chart

Clinical Monitoring during LTBI Treatment

Provide education and discuss monitoring plan with patients at treatment initiation.

Patients should be evaluated monthly for:
- Adherence to the prescribed regimen
- Signs and symptoms of TB disease

Adverse reactions:

Evidence of hepatotoxicity such as:
- Nausea or vomiting
- Abdominal pain or tenderness (especially in right upper quadrant)
- Anorexia
- Jaundice

Other adverse reactions such as:
- Fever
- Rash
- Persistent paresthesia
- Fatigue ≥3 days
- Easy bruising/bleeding
- Arthralgia

Systemic drug reactions and influenza-like syndromes are usually self-limiting and mild but can rarely include severe reactions such as syncope and hypotension (more frequently associated with the 12-dose isoniazid/rifapentine regimen).
If adverse reactions occur, a prompt clinical evaluation is necessary with treatment changes as indicated.

(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)

Adverse Reactions
Adult Treatment Regimen
Infant, Child, or Adolescent Treatment Regimen
Lab Monitoring
Treatment Completion

Return to LTBI Flow Chart

Groups at Risk of Developing TB

If the answer to any of the below questions is "yes," this patient should be tested for TB infection. If all the below questions are answered "no," this patient is at low risk for TB disease, and should not be tested at this time. If, at any time in the future, such a patient develops any of the below risk factors, they should then be tested for TB infection.

Individuals Recently Infected	Individuals with Clinical Conditions
• Close contacts of persons with infectious TB disease • Persons who have immigrated within the last 5 years from areas with high TB rates (Any country other than the United States, Canada, Australia, New Zealand, or those in western or northern Europe is considered a high incidence area) • Persons with prolonged stay (>1 month) in areas with high TB rates (Any country other than the United States, Canada, Australia, New Zealand, or those in western or northern Europe is considered a high incidence area) • Persons who live or work in clinical or institutional settings where TB exposure may be likely (e.g., hospitals, prisons, homeless shelters, nursing homes, mycobacteriology labs, medical waste management facilities) • Children less than 5 years of age exposed to adults in high risk-categories	• Persons with HIV infection • Persons with evidence of old, healed TB lesions on chest X-ray • Persons with low body weight (<90% of ideal body weight) • Persons with certain medical conditions (e.g., silicosis, chronic renal failure, diabetes mellitus, some cancers, gastrectomy/jejunoileal bypass, organ transplant) • Persons receiving immunosuppressive therapy e.g. prolonged corticosteroid therapy (the equivalent of >15 mg/d of prednisone for one month or more], TNF-α blockers) • People who inject drugs

More Information on TB and Diabetes: https://www.cdc.gov/tb/topic/basics/tb-and-diabetes.html

(CDC, *Who Should Be Tested for TB Infection* 2016)
(CDC, Core Curriculum on TB 2021)

Should this Patient Be Tested for TB Infection?

Return to LTBI Flow Chart

Comparison of the Interferon-Gamma Release Assay and Tuberculin Skin Test

IGRA	TST
In vitro test, indirect	*In vivo* test, indirect
More specific antigens	Less specific antigens
Requires a blood test	Requires an intradermal test
Detects interferon-gamma release	Interpreted by induration, not erythema
A prior IGRA does not boost a subsequent IGRA; a prior TST can boost the IGRA after 72 hours and up to 6 months	A prior TST can boost a subsequent TST or IGRA
1 to 2 patient visits	2 to 4 patient visits
Fixed interpretation criteria	Risk-stratified interpretation
Results in 1 to 2 days (although batching extends the turnaround time)	Results in 2 to 3 days (10 days for two-step testing)
Not affected by BCG or most non-tuberculous mycobacteria	Cross-reacts with BCG and non-tuberculous mycobacteria
Standard laboratory reporting in medical records	Variability in where results are recorded

(National Society of Tuberculosis Clinicians, *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations* 2021)

Types of TB Tests and Which to Use

Return to LTBI Flow Chart

IGRAs available in the United States

QuantiFERON™ – *TB* Gold Plus (QFT-Plus)	T-SPOT™ *TB*
Results reported as positive, negative, or indeterminate.	Results reported as positive, negative, invalid, or borderline.
Indeterminate results: Do not have diagnostic interpretation; may be a result of an error in performing the test or immunosuppression. Repeat IGRA or administer TST.	**Invalid results:** Do not have diagnostic interpretation; may be a result of testing/laboratory issues, patient health or improper specimen handling. Repeat IGRA or administer TST. **Borderline results:** Quantitative values are near but not reaching the threshold for positivity and result interpretation will depend on patient risk factors. In general, the test should be repeated.
Link: https://www.quantiferon.com/us/products/quantiferon-tb-gold-plus-us/package-inserts	**Link:** https://www.tspot.com/wp-content/uploads/2019/12/PI-TB-US-0001-V7.pdf

(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)

Types of TB Tests and Which to Use

Return to LTBI Flow Chart

Interpretation of TB Blood Test Results

TB Blood Test Result	Interpretation
Positive	*M. tuberculosis* infection likely.
Negative	*M. tuberculosis* infection unlikely, but cannot be excluded, especially if: 1. Patient has signs and symptoms consistent with TB disease. 2. Patient has a high risk for developing TB disease once infected with *M. tuberculosis* (e.g., the patient is immunosuppressed).
Indeterminate (QFT-Plus only) or Invalid (T-Spot only)	The test did not provide useful information about the likelihood of *M. tuberculosis* infection. Repeating a TB blood test or performing a TST may be useful.
Borderline (T-Spot only)	Repeating a TB blood test or performing a TST may be useful.

(CDC, LTBI: A Guide for Primary Health Care Providers 2021)

Expert consultation is suggested when test results are inconsistent with the clinical picture (e.g., positive tests in persons with low risk), borderline T-SPOT.TB results or results close to the cut point with QFT-Plus.

Types of TB Tests and Which to Use

Return to LTBI Flow Chart

Interpretation of Tuberculin Skin Test (TST) Reactions

5 or more millimeters	10 or more millimeters	15 or more millimeters
A TST reaction of ≥5 mm of induration is considered positive for: • People living with HIV • Recent contacts of people with infectious TB • People with chest x-ray findings suggestive of previous TB disease • People with organ transplants • Other immunosuppressed patients (e.g., patients on prolonged therapy with corticosteroids equivalent to/greater than 15 mg per day of prednisone or those taking TNF-alpha antagonists)	A TST reaction of ≥10 mm of induration is considered positive for: • People born in countries outside of the United States, Canada, Australia, New Zealand, or countries outside in northern or western Europe • People who abuse drugs • Mycobacteriology laboratory workers • People who live or work in high-risk congregate settings (e.g., nursing homes, homeless shelters, or correctional facilities) • People with certain medical conditions that place them at risk for TB (e.g., silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, or certain intestinal conditions) • People with a low body weight (less than 90% of ideal body weight) • Children younger than 5 years of age • Infants, children, and adolescents exposed to adults in high-risk categories	A TST reaction of ≥15 mm of induration is considered positive for: • People with no known risk factors for TB

(CDC, LTBI: A Guide for Primary Health Care Providers 2021)

Types of TB Tests and Which to Use

Return to LTBI Flow Chart

Differentiating Between LTBI and TB Disease

LTBI	TB Disease
• No symptoms or physical findings suggestive of TB disease • TB blood test or TST result usually positive • Chest radiograph is typically normal • If done, respiratory specimens are smear and culture negative • Cannot spread TB bacteria to others • Should consider treatment for LTBI to prevent TB disease	• Symptoms may include one or more of the following: fever, cough, chest pain, weight loss, night sweats, hemoptysis, fatigue, and decreased appetite • TB blood test or TST result usually positive • Chest radiograph is usually abnormal, but may be normal in people with advanced immunosuppression or extrapulmonary TB disease • Respiratory specimens are usually smear and/or culture positive, but may be negative in people with extrapulmonary TB disease or minimal/early pulmonary TB disease • Can spread TB bacteria to others

(CDC, *Latent TB infection and TB disease* 2020)
(CDC, LTBI: A Guide for Primary Health Care Providers 2021)

Does This Patient Have Active TB Disease?

Return to LTBI Flow Chart

Patient Adherence and Education

- Educate patients about importance of good adherence at treatment initiation and throughout treatment
- Explain possible side effects and adverse drug reactions and provide patients with written information
- Advise to promptly seek medical evaluation for adverse reactions and provide guidance for when to stop treatment in the case of serious adverse reactions

Support Adherence

Identify barriers by assessing for:

- appointment conflicts
- misinformation about TB
- health beliefs and practices
- limited financial resources
- co-morbidities
- side effects
- language barriers, and stigma

Collaborate with local health department and other consultation resources as needed.
Provide effective patient-centered education with opportunities to bring up concerns or questions.
Discuss pill burden with the patient; provide information on short course treatment regimens as appropriate.

(Center of Disease Control, LTBI: A Guide for Primary Health Care Providers 2021)
(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)

Treatment Considerations

Return to LTBI Flow Chart

<table>
<tr><th colspan="4">Adult Treatment Regimens for LTBI</th></tr>
<tr><th>Regimen</th><th>Adult Dosage</th><th>Completion Criteria</th><th>Use in Adults</th></tr>
<tr><td>3 Months of Once-Weekly Isoniazid (INH) Plus Rifapentine (3HP)

PREFERRED</td><td>Isoniazid:
15 mg/kg rounded to nearest 50 or 100 mg; 900 mg max.

Rifapentine:<table><tr><th>Weight (kg)</th><th>Dose (mg)</th></tr><tr><td>25.1-32.0</td><td>600</td></tr><tr><td>32.1-49.9</td><td>750</td></tr><tr><td>≥50</td><td>900 max.</td></tr></table></td><td>12 doses within 16 weeks</td><td>• Recommended for all adults, including people living with HIV (as drug interactions allow)
Not indicated for:
• Persons with M.tuberculosis infection that is presumed resistant to INH and/or rifampin
• Persons who had prior adverse events or hypersensitivity to INH, rifampin, or rifapentine
• People who are pregnant or expecting to become pregnant</td></tr>
<tr><td>4 Months of Daily Rifampin (4R)

PREFERRED</td><td>10 mg/kg; 600 mg max.</td><td>120 doses within 6 months</td><td>• Recommended for HIV-negative adults
• Careful consideration is recommended when using this regimen in severely immunosuppressed persons</td></tr>
<tr><td>6 or 9 Months of Daily Isoniazid (6H/9H)</td><td>5 mg/kg; 300 mg max.</td><td>6 months: 180 doses within 9 months
9 months: 270 doses within 12 months</td><td>• 6 months of INH is recommended for treatment of all adults
• 9 months of INH is also acceptable
• May be used when preferred regimens are contraindicated</td></tr>
<tr><td>3 Months of Daily Isoniazid Plus Rifampin

Consultation prior to use suggested/ recommended</td><td>Isoniazid 5 mg/kg; 300 mg max.

Rifampin 10 mg/kg; 600 mg max.</td><td>90 doses within 4 months</td><td>Recommended for all adults, including people living with HIV (as drug interactions allow)</td></tr>
</table>

(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)
(Sterling et al., *Guidelines for the treatment of latent tuberculosis infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020*)

LTBI Treatment Regimens
Infant, Child, or Adolescent Treatment Regimen
Treatment Completion
Return to LTBI Flow Chart

Infant, Children and Adolescent Treatment Regimens for LTBI				
Drug(s)	**Formulation**	**Duration/Total Doses**	**Frequency**	**Dose**
Isoniazid (INH) **and** **Rifapentine (RPT)** **(3HP)** **PREFERRED**	100 or 300 mg tablets 150 mg tablets in a blister pack[a]	3 months/12 doses	Once weekly[b]	**Children aged 12 years and older:** **INH:** 15 mg/kg rounded up to the nearest 50 or 100 mg; max. 900 mg **RPT:** 10-14.0 kg: 300 mg 14.1-25.0 kg: 450 mg 25.1-32.0 kg: 600 mg 32.1-49.9 kg: 750 mg ≥50.0 kg: 900 mg max. 900 mg
				Children aged 2-11 years: **INH:** 25 mg/kg; rounded up to the nearest 50 or 100 mg; max. 900 mg **RPT:** 10-14.0 kg: 300 mg 14.1-25.0 kg: 450 mg 25.1-32.0 kg: 600 mg 32.1-49.9 kg: 750 mg ≥50.0 kg: 900 mg max. 900 mg
Rifampin (RIF) **(4R)** **PREFERRED**	150 or 300 mg capsules	4 months/120 doses	Daily	**Infants, children, and adolescents:** 15-20 mg/kg[c]; max. 600 mg
Isoniazid (INH) **(9H)**	100 or 300 mg tablets	9 months/270 doses	Daily	**Infants, children, and adolescents:** 10-15 mg/kg; max. 300 mg
		9 months/76 doses	Twice weekly[d]	**Infants, children, and adolescents:** 20-30 mg/kg; max. 900 mg **(Must be given with DOT)**

Isoniazid (INH) **and** **Rifampin (RIF)** **Consultation prior to use suggested/ recommended**	100 or 300 mg tablets 150 or 300 mg capsules	3 months/ 90 doses	Daily	**Infants, children, and adolescents:** **INH:** 10-15 mg/kg; max. 300 mg **Infants, children, and adolescents:** **RIF:** 15-20 mg/kg[c]; max. 600 mg

When given as part of 4-drug therapy for suspected TB disease later found to be TB infection only. Due to an increased risk of hepatotoxicity with a regimen consisting of only RIF and PZA, this option should NOT be used outside of a four-drug regimen.

a. Blister pack should be kept sealed until use.

b. The INH-RPT regimen can be provided via directly observed therapy (DOT) or self/family administration. The choice is based on local practice, individual patient attributes and preferences, and other considerations, including risk for progression to TB disease, especially severe forms such as disseminated TB or TB meningitis. Because of this risk, many experts prefer to collaborate with health departments to provide this regimen to children using DOT.

c. The AAP notes that many experts recommend using a daily RIF dose of 20-30 mg/kg/day for infants and toddlers.[4]

d. The INH twice weekly regimen must be provided via DOT

Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider: 2020 (inclusive page numbers). This guide is available at
(Ahamed et al., *Management of Latent Tuberculosis Infection in Children and Adolescents* 2019)
(Sterling et al., *Guidelines for the treatment of latent tuberculosis infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020*)

Is your patient HIV+? Click the following links below for more resources about medication.

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV:
https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/tuberculosishiv-coinfection

*Visit https://hivinfo.nih.gov for the latest guidelines and complete list of contraindications.
Mycobacterium tuberculosis Infection and Disease | NIH (hiv.gov)

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/tuberculosishiv-coinfection

https://www.cdc.gov/tb/topic/treatment/ltbi.htm

Formulation and Special Considerations for Pediatric Patients

LTBI Treatment Regimens

Treatment Completion

Return to LTBI Flow Chart

Formulation and Special Considerations for Pediatric Patients

Isoniazid (INH): 100 mg and 300 mg tablets

A liquid preparation is also available or can be compounded by a pharmacy, but contains sorbitol which can cause diarrhea, abdominal pain, or cramping and, therefore, is generally not recommended.

Techniques for administration:

- For children unable to swallow tablets, the INH tablets should be crushed and dissolved in a few drops of warm water to create a slurry, then mixed with a small amount of semi-soft food the child likes (e.g., mashed bananas, or sugar-free applesauce, pudding, or yogurt).
- The crushed medication slurry should be mixed with the smallest amount of food possible to ensure the child consumes the entire dose.
- Afterwards, a spoonful of food without medicine should be given, followed by liquid to wash down the INH. For accurate dosing, do not add crushed medication to a full glass of water or milk, as the drug will sink to the bottom.
- The technique of crushing and mixing with food is generally successful and can be used in most children.

Rifapentine (RPT): 150 mg tablets packed in blister packs

- Packs should be kept sealed until use.
- May not be readily available at commercial pharmacies.

Techniques for administration:

- Methods of administration for RPT in children have not been standardized, however, the above process of crushing, creating a slurry, and mixing medication with the smallest amount of food possible (that the child likes) may be used.
- Administering RPT with food increases bioavailability, although current recommendations do not address whether the INH-RPT regimen should be given with food.

Adverse effects and drug interactions:

- For severe adverse reactions in children, including hepatoxicity, treatment should be discontinued, and supportive medical care provided as needed. Consultation with a pediatric TB specialist is recommended for restarting and managing treatment.

Report adverse events from LTBI treatment to FDA Medwatch at www.accessdata.fda.gov/scripts/medwatch/index.cfm **or 1-800-FDA-1088 and the CDC Division of Tuberculosis Elimination at** ltbidrugevents@cdc.gov

(Ahamed et al., *Management of Latent Tuberculosis Infection in Children and Adolescents* 2019)

Infant, Child, or Adolescent Treatment Regimen

Treatment Completion

Return to LTBI Flow Chart

Directly Observed Therapy (DOT)

- Practitioners should consider using DOT for LTBI patients at high risk that may have difficulty adhering to a treatment regime.
- DOT is specifically recommended for patients that face barriers to adherence: young children, chronically homeless, mentally ill, substance use issues, or cognitive impairment.
- Video directly observed therapy (vDOT) is another option available for providers to assist patients. This may provide more flexibility for patients and providers in scheduling DOT.
- Practitioners should consult their local health department if they believe a LTBI patient requires DOT.

(National Society of Tuberculosis Clinicians, *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations* 2021)

Treatment Considerations

Return to LTBI Flow Chart

Adverse Drug Interactions (ADRs) and Considerations for All Regimens

Adverse Drug Reactions

Serious adverse drug reactions are rare. The risk of hepatotoxicity is minimal in most patients and should not deter treatment. However, periodic monitoring is recommended. In case of possible severe ADRs, discontinue treatment and provide supportive medical care as indicated.

Isoniazid: Hepatic enzyme elevation, rash, peripheral neuropathy, mild CNS effects.

Rifampin and rifapentine: GI intolerance, hepatitis, bleeding problems (from gums or other sites), easy bruising, flu-like symptoms.

More commonly associated with 12-dose isoniazid/rifapentine regimen: Hematologic toxicity, hypersensitivity reaction (e.g., hypotension or thrombocytopenia).

Considerations for Treatment

- Rifamycin-based regimens should be used whenever possible, based on individual patient attributes and preferences including potential for drug-drug interactions, local practice, and drug susceptibility results of the presumed source case, if known.
- 6 or 9 month INH regimens have lower treatment completion rates than shorter-rifamycin based regimens, but may be used when the preferred regimens are contraindicated due to intolerance, resistance, or drug interactions.
- Rifamycin-associated drug interactions include, but are not limited to, hormonal contraceptives, certain HIV antiretrovirals, methadone, and anticoagulants.
- Weekly rifapentine has fewer drug interactions than rifabutin, which has fewer interactions than rifampin; thus the 12-dose rifapentine containing regimen can be considered when rifampin is contraindicated.
- Rifabutin has a lower drug interaction profile than rifampin; to minimize drug-drug interactions, consider use of rifabutin in place of rifampin in the 4-month rifampin regimen.
- See https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/overview for current guidelines on treatment for LTBI in people living with HIV and information on drug-drug interactions with HIV antiretrovirals.
- Hepatitis risk increases with age, alcohol use, and concurrent use of other hepatotoxic drugs.
- Potential for acquired drug resistance if TB disease is not adequately excluded is an important consideration for all regimens.
- In any persons with severe immunosuppression (e.g., those on biologic response modifiers such as TNF-α antagonists or those living with HIV who have low CD4 lymphocyte counts), there is an increased risk of subclinical, atypical, or asymptomatic disease. Rifampin resistance could develop if a person is inadvertently treated with rifampin monotherapy for LTBI, when they have TB disease.
- People who become pregnant while on LTBI treatment should consult their provider.
- If interruptions in therapy occur such that patients cannot complete treatment within the recommended time frame, treatment should be restarted, after a careful evaluation for TB disease.

Patients on INH containing regimens:

- Pyridoxine (vitamin B6) should be added for pregnant people, patients with malnutrition, alcoholism, diabetes, and those with other conditions associated with neuropathy. Give 50 mg/week with the 12-dose isoniazid-rifapentine regimen and 25–50 mg/day with other INH containing regimens.

Patients on rifamycin containing regimens:

- Patients should be educated that temporary orange discoloration of urine, sweat, tears, and other bodily fluids is a normal and expected side effect.
- People who use hormonal birth control should be instructed to **add, or switch to a barrier method.**

(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)

Clinical Monitoring During LTBI Treatment

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Laboratory Monitoring

Routine monthly monitoring of liver function tests (LFTs) is not generally indicated.

Baseline LFTs are indicated for those:

- With a history of liver disease or liver disorders
- Living with HIV
- Who regularly use alcohol
- Who are pregnant or less than 3 months postpartum
- Taking other potentially hepatotoxic drugs (e.g., anti-convulsants) or over-the-counter drugs (e.g., acetaminophen)

LFT monitoring based on clinical scenario is indicated for:

- Persons at risk for, or with a history of liver disease
- Persons who have abnormal baseline LFTs
- Those who develop symptoms consistent with hepatotoxicity.

Medications should be withheld, and patients evaluated if:

- Transaminase levels ≥3 times upper limit of normal in presence of symptoms
- Transaminase levels ≥5 times upper limit of normal in asymptomatic patients

When LFTs have returned to normal, consider an alternate regimen, with close clinical and laboratory monitoring. Consult a TB expert.

Report adverse events to CDC Division of Tuberculosis Elimination by sending an email to ltbidrugevents@cdc.gov **and to FDA MedWatch at** accessdata.fda.gov/scripts/medwatch/index.cfm **or 1-888-INFO-FDA)**
(Rutgers Global TB Institute, Diagnosis, and treatment of latent tuberculosis infection (LTBI) in adults 2021)

Clinical Monitoring During LTBI Treatment

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Interruptions in Therapy

Providers should ask parents or caregivers about planned extended vacations or absences and take this into consideration when starting treatment for LTBI. When interruptions in treatment do occur, providers should attempt to determine and address the reason for these lapses, including the regimen itself (e.g., intermittent versus daily therapy). Consultation with a pediatric TB expert is suggested. Check for medication shortages before determining a regimen.

Consider checking for medication shortages prior to prescribing medication. Choice of regimen impacted anticipated availability of medications. It is recommended to stay on the same medication throughout the treatment.

FDA Drug Shortage: https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages

Treatment Completion

Completion Time Lengths for Each Regimen

- Completion of treatment for Rifapentine and isoniazid once weekly is 12 doses within 16 weeks. (For patients who are unable to complete 12 doses, treatment can be considered complete if 11 doses are taken within 16 weeks.) Doses should be separated by >72 hours to be counted.
- Completion of treatment for 4 months of rifampin is 120 doses within 6 months.
- Completion of treatment for 9 months of isoniazid daily regimen is 270 doses within 12 months. For patients who are unable or unlikely to complete 270 doses, treatment may be completed if they have taken the number of doses in the time frame needed to complete the daily 6 months Isoniazid regimen below.
- Completion of treatment of isoniazid for 9 months, if dosing is twice weekly by DOT, is 76 doses within 12 months.
- Completion of treatment for 6 months of isoniazid daily is 180 doses within 9 months.
- Completion of treatment of isoniazid for 6 months, if dosing is twice weekly by DOT, is 52 doses within 9 months.

(National Society of Tuberculosis Clinicians, *Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations* 2021)

Examples of Treatment Completion Cards

Return to LTBI Flow Chart

Treatment Completion Cards

Below are two examples of treatment completion cards that can be given to a patient. It is important that a patient has some form of documentation as proof of their treatment.

Example 1 of Treatment Completion

RECORD OF TREATMENT COMPLETION

To Whom It May Concern: The following is a record of evaluation and treatment for *M. tuberculosis* infection:

Name: _____ **Date of birth:** _____

Tuberculin skin test (TST): **Date:** _____

Results (in millimeters of induration): _____

TB blood test: **Date:** _____ **Type of test:** _____ **Result:** _____

Chest radiograph: **Date:** _____ **Result:** _____

Date medication started: _____ **Date completed:** _____

Medication(s): _____

This person is not infectious. They may always have a positive TB test, so there is no reason to repeat the test. If you need any further information, please contact this office.

PROVIDER CONTACT INFORMATION

Name: _____

Phone number: _____

Address: _____

Signature of provider: _____

(CDC, *LTBI: A Guide for Primary Health Care Providers* | *Guides & Toolkits* 2021)

Example 2

Provider's Name
Office Address
Office Phone Number

Name: _____

Date of birth: _____

TST: _____ mm in duration **Date:** _____

IGRA QFT/T-Spot: ☐ Pos ☐ Neg ☐ Indeterminate
Date: _____

Chest xray date: _____
☐ Normal ☐ Abnormal

Name of Drug(s): _____

Started: _____ **Stopped:** _____

Completed treatment: ☐ Yes ☐ No
Mos. _____

Signature: _____

Return to LTBI Flow Chart

ICD-10 Codes

Below is a list of codes to ensure that you are reimbursed for treating LTBI patients.

ICD-10 Codes Related to LTBI Testing and Diagnosis

- Z11.7: Encounter for testing for LTBI
- Z86.15: Personal history of LTBI
- Z22.7: Diagnosis of LTBI
- R76.11: Nonspecific reaction to TST without active tuberculosis
- R76.12: Nonspecific reaction to cell-mediated immunity measurement of gamma interferon antigen response without active tuberculosis See International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) for the complete list of ICD-10 codes LTBI, latent tuberculosis infection; TST, Mantoux tuberculin skin test

Click the link to search for ICD-10 Codes: https://icd10cmtool.cdc.gov/?fy=FY2023
(CDC, ICD-10-CM 2022)

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Patient Education Resources

Providers should be educating their patients about TB. Education is beneficial to patient treatment adherence by answering questions about transmission, exposure, infection, testing, disease progression, and understanding the advantages of treatment. **Remember to communicate with patients in their preferred language and education level.**

Below are links to resources in multiple languages that will help with patient education:

Basic TB Education for Patients

- CDC Latent TB Education Resource Website
- Questions and Answers | Pamphlets, Brochures, Booklets | Publications & Products | TB | CDC
- Publications & Products | TB | CDC

Testing Education Resources for Patients

- TB Skin Testing for Tuberculosis (cdc.gov)
- Testing for Tuberculosis (TB) (cdc.gov)
- Tuberculosis Elimination (cdc.gov)

TB Regimen Education for Patients

- 12-Dose Regimen for Latent TB Infection-Patient Education Brochure | Pamphlets, Brochures, Booklets
- LTBI Treatment Information in a Variety of Languages: (3 months INH/Rifapentine, 4 months Rifampin, 9 months Isoniazid)

(CDC, *Latent tuberculosis infection resources* 2022)

Treatment Considerations

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Consultation

Expert consultation is available from state or local health departments; consultation is recommended for diagnosis of TB disease or of LTBI in complex clinical situations (e.g., those on or about to start immunosuppressive therapy).

NYSDOH TB Control: 1-518-474-7000

Regional Center of Excellence: The experts at the Regional Center for Excellence can answer Provider's questions. **https://globaltb.njms.rutgers.edu/tb_consultation/index.php**

CDC Online LTBI Resource Hub: Latent Tuberculosis Infection Resources

Return to LTBI Flow Chart

Document Forms for Patients

Examples:

Record of TB Blood Test

To Whom It May Concern:

The following is a record of TB blood test results:

Name: _____

Date of birth: _____

Type of test: _____ Date blood collected: _____

Laboratory: _____

For QFT-Plus*:	**For T-SPOT®.*TB*:**
Nil: _____ IU/mL	Nil: _____ spots
TB1: _____ IU/mL	TB Panel A: _____ spots
TB1 minus Nil: _____ IU/mL	TB Panel A minus Nil: _____ spots
TB2: _____ IU/mL	TB Panel B: _____ spots
TB2 minus Nil: _____ IU/mL	TB Panel B minus Nil: _____ spots
Mitogen: _____ IU/mL	Mitogen: _____ spots
Mitogen minus Nil: _____ IU/mL	T-Spot Interpretation _____
QFT-Plus Interpretation _____	

Record of Tuberculin Skin Test

To Whom It May Concern:

The following is a record of Mantoux tuberculin skin test (TST) results:

Name: _____ Date of birth: _____

Date and time test administered: _____

Administered by: _____

Manufacturer of Purified Protein Derivative (PPD): _____

Expiration date: _____ Lot number: _____

Time test read: _____ Read by: _____

Date: _____ Induration: _____ mm

TST interpretation: _____

(CDC, *LTBI: A Guide for Primary Health Care Providers | Guides & Toolkits* 2021)

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